
**ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ**

**ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ**


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**ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ**

# Assessment of the reporting quality of RCTs for sodium valproate in status epilepticus published from 2007 to 2018 based on the CONSORT statement.

# Αξιολόγηση της ποιότητας καταγραφής των δημοσιευμένων από το 2007 έως το 2018 τυχαιοποιημένων κλινικών δοκιμών που αφορούν στη χρήση Βαλπροϊκού Νατρίου στην Επιληπτική Κατάσταση με βάση τη δήλωση CONSORT.


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# Contents

# Abstract

**Introduction:**Status Epilepticus(SE) is a medical emergency associated with significant morbidity and mortality. Randomized controlled trials(RCTs) are important means in appraising therapeutic interventions. Evaluation of the reporting quality of RCTs regarding the use of second line antiepileptic drugs(AEDs) in SE treatment is insufficient.

**Purpose:**The implementation of the CONSORT statement in the assessment of the reporting quality of RCTs for sodium valproate(VPA) in SE published from 2007 to 2018.

**Methods:**A literature search was conducted in MEDLINE(PubMed) and Cochrane Library, as well as a manual search of cited references in the retrieved RCTs and meta-analyses. Our primary objective was to estimate the proportion of adherence to the CONSORT statement. Secondary objectives included the investigation of possible associations with the reporting quality of abstracts and journal impact factor(IF), plus the determination of the proportion of adherence per CONSORT-item. We additionally assessed the reporting quality of Pilot RCTs.

**Results:**Seven eligible studies were identified. Mean adherence was 52.40% (sd=16.57,median=47%). According to non-parametric analysis, correlation between reporting quality of abstracts and articles was significant(Spearman's rho=0.829,p-value=0.021<0.05, Pearson's r=0.737,p-value=0.059>0.05). Correlation between CONSORT adherence and journal ranking was insignificant (rho=0.571,p-value=0.180>0.05, r=0.627, p-value=0.183). Introduction and Discussion items were more adequately reported compared to methodological features and outcomes. CONSORT compliance between RCTs and Pilot RCTs(n=four, mean adherence=55.05%, sd=7.48,median=61.11%) did not differ significantly according to Mann-Whitney-U test(p-value=0.85).

**Conclusions:**Adherence to the CONSORT statement abstains from the desirable standard. Principally, items concerning methods and results fail to reach a satisfying level of reporting.



**Key-words:** status epilepticus, sodium valproate, CONSORT statement, Randomised Control Trial

# Περίληψη

**Εισαγωγή:**Η επιληπτική κατάσταση(ΕΚ) αποτελεί ιατρικό επείγον που σχετίζεται με υψηλή νοσηρότητα και θνητότητα. Οι τυχαιοποιημένες κλινικές δοκιμές (ΤΚΔ) είναι εξαιρετικά σημαντικό εργαλείο στην αξιολόγηση των θεραπευτικών παρεμβάσεων. Η ποιότητα της καταγραφής στις ΤΚΔ που αφορούν τη χρήση δεύτερης γραμμής αντιεπιληπτικών στην ΕΚ δεν έχει εκτιμηθεί επαρκώς.

**Σκοπός:**Η εφαρμογή της δήλωσης CONSORT στην αξιολόγηση της ποιότητας καταγραφής των δημοσιευμένων από το 2007 έως το 2018 ΤΚΔ που αφορούν στη χρήση Βαλπροϊκού Νατρίου(ΒΠΝ) στην ΕΚ.

**Μέθοδος:**Πραγματοποιήσαμε αναζήτηση στις βάσεις δεδομένων MEDLINE(PubMed), και Cochrane Library, καθώς επίσης, χειροκίνητη αναζήτηση στη βιβλιογραφία κάθε ΤΚΔ και μετα-ανάλυσης που ανακτήθηκε. Ως πρωταρχικός στόχος τέθηκε ο υπολογισμός του ποσοστού εναρμόνισης κάθε ΤΚΔ με τη δήλωση CONSORT. Δευτερεύοντες στόχοι ορίστηκαν ο καθορισμός πιθανών συσχετίσεων με το ποσοστό συμμόρφωσης των περιλήψεων στην επέκταση της δήλωσης CONSORT για τις περιλήψεις και τον συντελεστή βαρύτητας περιοδικού, καθώς και ο προσδιορισμός του ποσοστού των μελετών που καταγράφουν το κάθε ζητούμενο. Επιπλέον, υπολογίστηκε η ποιότητα καταγραφής των Πιλοτικών ΤΚΔ.

**Αποτελέσματα:**Εντοπίστηκαν επτά μελέτες που πληρούσαν τις προϋποθέσεις. Η μέση εναρμόνιση υπολογίστηκε 52.40%(τυπική απόκλιση=16.57,διάμεσος=47%). Ο μη παραμετρικός έλεγχος ανέδειξε σημαντική συσχέτιση μεταξύ της ποιότητας καταγραφής περιλήψεων και άρθρων(Spearman's rho=0.829,p-value=0.021<0.05, Pearson’s r=0.737,p-value=0.059>0.05). Δεν αναδείχθηκε σημαντική συσχέτιση με τον συντελεστή βαρύτητας των περιοδικών(rho=0.571,p-value=0.180>0.05, r=0.627, p-value=0.183). Η καταγραφή ήταν αρτιότερη στα τμήματα εισαγωγή και συζήτηση σε σχέση με τη μεθοδολογία και την παρουσίαση των αποτελεσμάτων. Η ποιότητα καταγραφής δε διέφερε σημαντικά μεταξύ ΤΚΔ και Πιλοτικών ΤΚΔ(n=4, μέση εναρμόνιση=55.05%,τυπική απόκλιση=7.48,διάμεσος=61.11%) σύμφωνα με το Mann-Whitney-U test(p-value=0.85).

**Συμπεράσματα:**Το ποσοστό συμμόρφωσης στη δήλωση CONSORT απέχει από το επιθυμητό επίπεδο. Κατά κύριο λόγο, η καταγραφή υστερεί ως προς τις μεθόδους και τα αποτελέσματα.



**Λέξεις κλειδιά:** επιληπτική κατάσταση, βαλπροϊκό νάτριο, δήλωση CONSORT, τυχαιοποιημένη κλινική δοκιμή,

# Introduction

Randomized Control Studies (RCTs) are the cornerstone of evidence-based medicine [1]. Ensuring the implementation of high quality standards in RCTs is essential in order to obtain solid evidence and derive valid conclusions. On the contrary, low quality RCTs may distort the results of an intervention prompting into misguided clinical decisions [2, 3].

The CONsolidated Standards Of Reporting Trials (CONSORT) statement was developed to improve the quality of reporting of RCTs [4, 5]. It comprises of a 25-item checklist and a flow diagram that ensure clarity and completeness of reporting [6]. Transparency of reporting is required for the reader to appraise the quality of the study and provides future researchers with the necessary information to replicate a study. Reports often omit important details. Deficient reporting likely reflects erratic conduction and commonly leads to misinterpretation of the study results [7].

The CONSORT statement was initially introduced in 1996[8] and underwent 2 revisions, in 2001 [9] and 2010 [10]. The revisions were accompanied by a detailed explanation and elaboration document [11, 12]. The CONSORT statement is endorsed by many scientific journals in order to improve the quality of RCTs [13-15]. Nonetheless it is important to remember that quality of reporting does not always align with methodological quality [16].

Epilepsy is a chronic condition in which a person suffers from recurrent seizures. Seizures constitute episodes of excessive electrical activity in the brain resulting in dysfunction of the structures involved [17]. Status epilepticus (SE) refers to seizures lasting more than 5 to 10 minutes or two or more consecutive seizures without recovery of full consciousness. A more practical approach suggests that SE is considered a situation in which seizure duration necessitates the use of antiepileptic drugs (AEDs). SE is officially classified into four categories, early SE (ErSE), established SE (EsSE), refractory SE (RSE) and super refractory SE (SRSE) [18].

It is recommended that initial treatment of SE relies on benzodiazepines. Established SE is defined as SE refractory to benzodiazepine treatment. EsSE persists for more than 30 minutes and is usually associated with permanent neuronal injury. Treatment of established SE requires admission to an Intensive Care Unit (ICU) and deployment of second line AEDs which include phenytoin (PHT), sodium valproate (VPA), levetiracetam(LEV), lacosamide and phenobarbital. Refractory and super refractory SE refer to episodes that render the use of intravenous anaesthetics necessary [19, 20].

SE is a medical emergency associated with significant morbidity and mortality [21]. Favourable prognosis is directly correlated with rapid seizure termination. Undoubtedly, it is of utmost importance to determine the most effective treatment plan, which has yet to be accomplished. Major controversy arises with regards to the efficacy and tolerability of second line AEDs [22]. As part of the effort to establish the most effective treatment plan, the number of studies testing VPA in SE is constantly increasing.

Nevertheless, assessment of the reporting quality of the studies is insufficient. To our knowledge, although benzodiazepines (first line AEDs) have been appraised in terms of reporting quality[23, 24], our study is the first to endeavour the evaluation of the reporting quality of RCTs for one second line AED, VPA, in SE treatment.

# Methods

We carried out a retrospective evaluation of RCTs on the subject of VPA use in the treatment of SE between January 1, 2007, and July 21, 2018.

**Search Method**

We performed a comprehensive search of the MEDLINE and Cochrane Library databases to identify all relevant RCTs published between January 1, 2007, and July 21, 2018. The search strategy used the MeSH terms ‘status epilepticus’ and ‘sodium valproate’ plus the terms ‘status epilepticus’, ‘epileptic status’, ‘valproate’ and ‘valproic acid’ as title or abstract words combined with the Boolean Operators ‘OR’ and ‘AND’.

(((((status epilepticus[MeSH Terms]) OR status epilepticus[Title/Abstract]) OR epileptic status[Title/Abstract]) AND ( "2007/01/01"[PDat] : "2018/07/21"[PDat] ))) AND ((((valproic acid[MeSH Terms]) OR valproate[Title/Abstract]) OR valproic acid[Title/Abstract]) AND ( "2007/01/01"[PDat] : "2018/07/21"[PDat] ))

The references quoted by retrieved RCTs as well as meta-analyses were manually searched.

**Eligibility Criteria**

We defined RCTs as prospective studies with random assignment of their human population to two or more intervention groups. We included reports that met the following criteria: (1) they were classified as RCTs (2) they were published from January 1, 2007 to July 21, 2018 (3) one intervention group was randomized to VPA (4) the population under research was people suffering from SE.

Exclusion criteria included: (1) reports not published in English (2) unavailable full articles (3) studies performed in animals (4) pilot studies (5) conference abstracts (6) study protocols (7) other study designs (eg retrospective study design, prospective not randomized design) (8) retracted papers.

We proceeded in a systematic review of all titles and abstracts retrieved. In case of inability to establish if a study met the inclusion criteria we reviewed the full text.

**Data Extraction**

The 2010 revised CONSORT statement comprises of 25 items, 12 of which are divided into 2 parts. Each of the 37 items was assessed equally by 1 point when adequately reported, 0 when either inadequately reported or absent and as not applicable according to certain features of the studies. Items reported more than once were assessed by 0 in case of inconsistency. Items composed of 2 or more sections were subdivided and valued equally (1/ number of sections) so as to assess the RCTs more accurately. Based on CONSORT 2010 explanation and elaboration document we decided to subdivide item 13a into 5 sections. Items 3b (changes to methods), 6b (changes to trial outcomes), 7b (interim analyses and stopping guidelines), 11b (description of the similarity of interventions), 12b (subgroup analyses and adjusted analyses), 14b (why the trial ended or was stopped), 18 (results of any other analyses performed) were not assessed in case of non-applicability. We determined the proportion of adherence to the CONSORT statement without taking not applicable items into consideration. Consequently, each study was rated against a different number of items.

**Table 1 | CONSORT 2010 checklist of information to include when reporting a randomised trial (adaptation after the addition of subdivisions)**

| Section/Topic | Item No | Checklist item | | | | |
|---|---|---|---|---|---|---|
| **Title and abstract** | 1a | Identification as a randomised trial in the title | | | | |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | | | | |
| **Introduction -** Background and objectives | 2a | Scientific background and explanation of rationale | | | | |
| | 2b | Specific objectives or hypotheses | | | | |
| **Methods** | | | | | | |
| Trial design | 3a | Description of trial design | Allocation ratio | | | |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | | | | |
| Participants | 4a | Eligibility criteria for participants | | | | |
| | 4b | Settings and locations where the data were collected | | | | |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | | | | |
| Outcomes | 6a | Completely defined pre-specified primary outcome measures, including how and when they were assessed | Completely defined pre-specified secondary outcome measures, including how and when they were assessed | | | |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | | | | |
| Sample size | 7a | How sample size was determined | | | | |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | | | | |
| Randomisation: | | | | | | |
| *Sequence generation* | 8a | Method used to generate the random allocation sequence | | | | |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | | | | |
| *Allocation concealment mechanism* | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | | | | |
| *Implementation* | 10 | Who generated the random allocation sequence | Who enrolled participants | Who assigned participants to interventions | | |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how | | | | |
| | 11b | If relevant, description of the similarity of interventions | | | | |
| Statistical methods | 12a | Statistical methods used to compare groups for primary outcomes | Statistical methods used to compare groups for secondary outcomes | | | |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | | | | |
| **Results** | | | | | | |
| Participant flow (a diagram is strongly recommended) | 13a | People evaluated for potential enrolment | Participants randomly assigned | Participants who completed treatment as allocated, by study group | Participants who completed follow-up as planned, by study group | Participants included in main analysis, by study group |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | | | | |
| Recruitment | 14a | Dates defining the period of recruitment | Dates defining the period of follow-up | | | |
| | 14b | Why the trial ended or was stopped | | | | |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | | | | |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | | | | |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group | For each primary and secondary outcome, the estimated effect size and its precision | | | |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | | | | |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | | | | |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | | | | |
| **Discussion** | | | | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | | | | |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | | | | |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | | | | |
| **Other information** | | | | | | |
| Registration | 23 | Registration number and name of trial registry | | | | |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | | | | |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | | | | |

Item 1b (Structured summary) was assessed separately based on the CONSORT for Abstracts extension [25], which comprises of 17 items. A 16-item version was deployed after the removal of the contact details item (specific to conference abstracts). 3 items were subdivided into 2 sections each valued with ½. Reported items inconsistent with the full text were assessed by 0. Item 1b was assessed by 1 when ≥8 of the 16 items were satisfied.

**Table 2 | Items to include when reporting a randomized trial in a journal or conference abstract**

| Item | Description | Subdivisions |
|---|---|---|
| Title | Identification of the study as randomized | |
| Authors * | Contact details for the corresponding author | |
| Trial design | Description of the trial design (e.g. parallel, cluster, non-inferiority) | |
| Methods | | |
| Participants | Eligibility criteria for participants and the settings where the data were collected | 1)eligibility criteria for participants<br>2)settings where the data were collected |
| Interventions | Interventions intended for each group | |
| Objective | Specific objective or hypothesis | |
| Outcome | Clearly defined primary outcome for this report | |
| Randomization | How participants were allocated to interventions | |
| Blinding (masking) | Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment | |
| Results | | |
| Numbers randomized | Number of participants randomized to each group | |
| Recruitment | Trial status | 1)recruitment status<br>2)follow up status |
| Numbers analysed | Number of participants analysed in each group | |
| Outcome | For the primary outcome, a result for each group and the estimated effect size and its precision | 1)a result for its group<br>2)the estimated effect size and its precision |
| Harms | Important adverse events or side effects | |
| Conclusions | General interpretation of the results | |
| Trial registration | Registration number and name of trial register | |
| Funding | Source of funding | |

**this item is specific to conference abstracts*

Further information collected included journal ranking for the publication year (according to the Journal IF published each summer by Clarivate Analytics (Thomson Reuters) via Journal Citation Reports), date of publication, CONSORT endorsement by the corresponding journal, country of origin, implementation of multicentre design, sample size, interventions assigned, prior use of first line treatment and targeted age group.

Due to the comparable number of retrieved RCTs and Pilot or Feasibility Trials we additionally decided to determine the proportion of adherence of pilot studies to the CONSORT extension for Pilot and Feasibility Trials[26] (26-item checklist). Evaluation was conducted on the same principles applied to the evaluation of RCTs. A 15-item checklist was utilised for the assessment of the item 1b(structured summary) and a threshold of 7.5/15 was set for the item to be considered as reported.

### Objectives

Our primary objective was to estimate the proportion of adherence to the CONSORT statement for each RCT. We describe the mean and median adherence, the standard deviation (SD), the minimum and maximum adherence.

Secondary objectives included the investigation of correlations between adherence to the CONSORT statement and adherence to the CONSORT extension for abstracts as well as Journal IF for the respective publication year. Furthermore, we determined the proportion of RCTs reporting each CONSORT-item. Additionally, we assessed the reporting quality of Pilot studies and proceeded to compare CONSORT compliance between RCTs and Pilot trials.

### Statistical Analysis

All statistical analyses were performed with SPSS Statistics Software Version 24. After calculating statistic measures of central tendency and dispersion, we proceeded to analysis of correlations through calculation of the Spearman's rank correlation coefficient (Spearman's rho, non parametric) and graphical presentation on scatter plots. In case of normally distributed data (according to the Shapiro-Wilk test which is superior to the Kolmogorov-Smirnov test for small samples)[27] we additionally determined the Pearson Correlation Coefficient (Pearson's r). Comparison between RCTs and Pilot trials was carried out through Mann-Whitney U test (in case of normality, independent-samples t-test was also calculated). A p-value of <0.05 was set to be significant.

## Results

The literature search identified 404 studies. The manual search did not provide us with additional RCTs. We meticulously screened all titles and abstracts retrieved and full texts when necessary. 7 studies [28-34] were considered eligible for our review and are included in the current study. The main characteristics of the studies are presented at table 3.

**Table 3 I Study characteristics**

| Study | Amiri at al | Su et al | Chitsaz et al | Malamiri et al | Gilad et al | Mehta et al | Agarwal et al |
|---|---|---|---|---|---|---|---|
| *Year Published* | 2018 | 2016 | 2013 | 2012 | 2008 | 2007 | 2007 |
| *Journals' IF** | 2.219[††] | 4.394 | ESCI[§] | 1.982 | 2.317 | 1.240 | 1.815 |
| *CONSORT endorsement*** | Yes | Yes | Yes | Yes | Yes | Yes | No |
| *Country* | Iran | China | Iran | Iran | Israel[§§] | India | India[§§] |
| *Centre design* | Single | Single | 2 centres | 2 centres | Not specified | Single | Not specified |
| *Sample size* | 110 | 73 | 30 | 60 | 74 | 40 | 100 |
| *Interventions* | VPA – PHT | VPA - Phenobarbital | VPA - PHT | VPA - Phenobarbital | VPA - PHT | VPA - Diazepam | VPA - PHT |
| *Initial use of first line AEDs(Benzodiazepines)* | Yes | Yes | Yes | Yes | No | Yes | Yes |
| *Significance of the results*[†] | No | Yes | No | No | No | No | No |
| *Population* | Adults | Adults | Adults and Children | Children | Adults | Children | Adults and Children |

* according to Journal IF published each summer by Clarivate Analytics (formerly Thomson Reuters) via Journal Citation Reports for the publication year

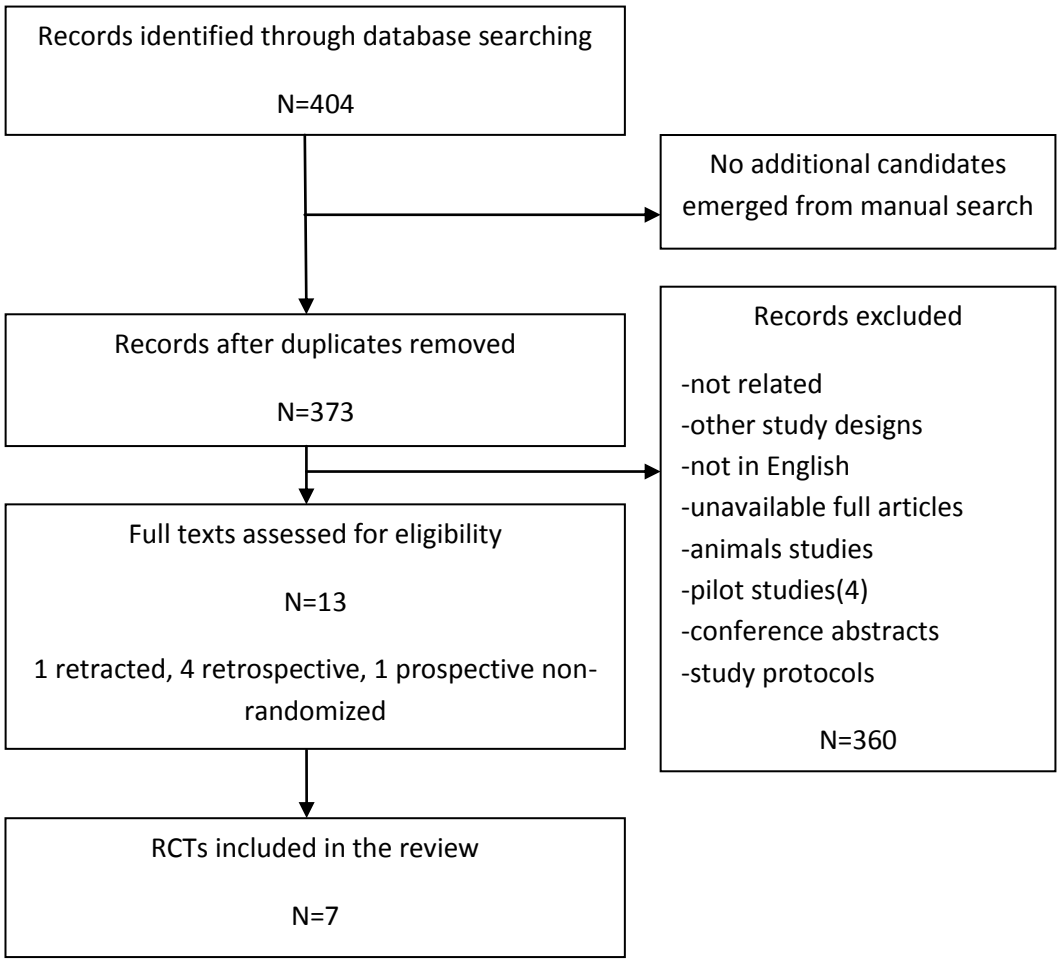
**according to the presently provided instructions to authors by each journal

[†]concerning primary outcome

[††]according to Journal IF published in year 2018 by Clarivate Analytics (formerly Thomson Reuters) via Journal Citation Reports which provides 2017 data. The 2018 data will be made available in the 2019 Journal Citation Reports release.

[§]emerging source citation index since 2015 [a new database within Clarivate Analytics' (formerly Thomson Reuters) Web of Science]. Journals indexed in the ESCI will not receive IF. However, the citations from ESCI will be included in the citation counts for the Journal Citation Reports
[§§]according to author information (not specified in the text)

**Figure 1 | Flow chart of the literature search**




**Consort Compliance**

Our primary purpose was to establish the proportion of consort adherence for each RCT. The following results were obtained:

Amiri at al: (14.10/30, 47%), Su et al (23.43/30, 78.1%), Chitsaz et al (10.60/32, 33.16%), Malamiri et al (21.60/30, 72%), Gilad et al (13.60/32, 42.5%), Mehta et al: (16.6/32, 51.86%), Agarwal et al: (13.50/32, 42.19%)

The mean CONSORT adherence was calculated at 52.40% with sd=16.57. The median was 47% and the minimum and maximum adherence 33.16% and 78.1% respectively.

Adherence per consort item was evaluated (table 4). Several items were assessed as not applicable overall (3b, 6b, 7b, 13b, 14b). Reporting of items 11b and 18 (subgroup analyses and adjusted analyses), 17b (both absolute and relative effect sizes) and 11b (applicable in solely one study) was null. Items 23 and 24 (trial registration and protocol), 13b (losses and exclusions after

randomisation), as well as 1b (evaluated according to CONSORT for Abstracts extension) were significantly underreported. As regards to item 10, two sections were completely omitted and section 'Who assigned participants to interventions' was reported in only one study. In contrast, items 2a and 2b (background and objectives), 5 (interventions) and 16 (number of participants included in each analysis) were reported in all 7 studies. Inconsistencies between abstract and full article reporting were detected in 2 studies (regarding eligibility criteria and primary outcome definition), whereas in 1 study's interpretation was not consistent with the results.

**Table 4 I Adherence per CONSORT item**

| Item | Reported %Frequency* | Not applicable | Item | Reported %Frequency* | Not applicable | Item | Reported %Frequency* | Not applicable |
|---|---|---|---|---|---|---|---|---|
| 1a | 57.14 | 0 | 8a | 28.57 | 0 | 15 | 42.86 | 0 |
| 1b | 14.3 | 0 | 8b | 57.14 | 0 | 16 | 100 | 0 |
| 2a | 100 | 0 | 9 | 28.57 | 0 | 17a | 42.86 | 0 |
| 2b | 100 | 0 | 10 | 4.76 | 0 | 17b | 0 | 0 |
| 3a | 71.43 | 0 | 11a | 57.14 | 0 | 18 | 0 | 3 |
| 3b | - | 7 | 11b | 0 | 6 | 19 | 85.71 | 0 |
| 4a | 71.43 | 0 | 12a | 71.43 | 0 | 20 | 42.86 | 0 |
| 4b | 71.43 | 0 | 12b | 0 | 3 | 21 | 85.71 | 0 |
| 5 | 100 | 0 | 13a | 65.71 | 0 | 22 | 85.71 | 0 |
| 6a | 57.14 | 0 | 13b | 14.3 | 0 | 23 | 14.3 | 0 |
| 6b | - | 7 | 14a | 64.27 | 0 | 24 | 14.3 | 0 |
| 7a | 28.57 | 0 | 14b | - | 7 | 25 | 42.86 | 0 |
| 7b | - | 7 | | | | | | |

*the denominator is determined by the trials in which the item is applicable

Participants flow was not illustrated in any of the studies by a flow diagram. Although, all 7 studies presented the number of participants randomized, treated as planned and analyzed, only one study reported the number of people evaluated for enrolment and participants followed up as planned.

**Figure 2 | CONSORT 2010 Flow Diagram**

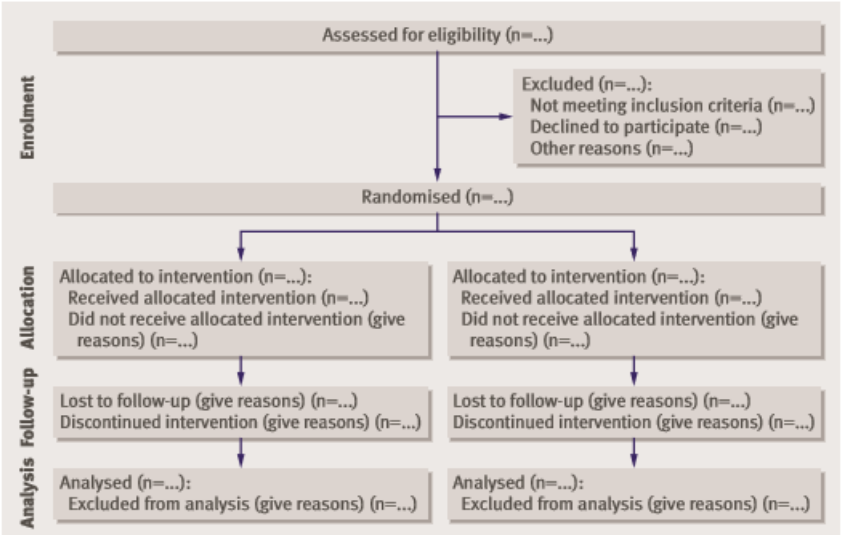
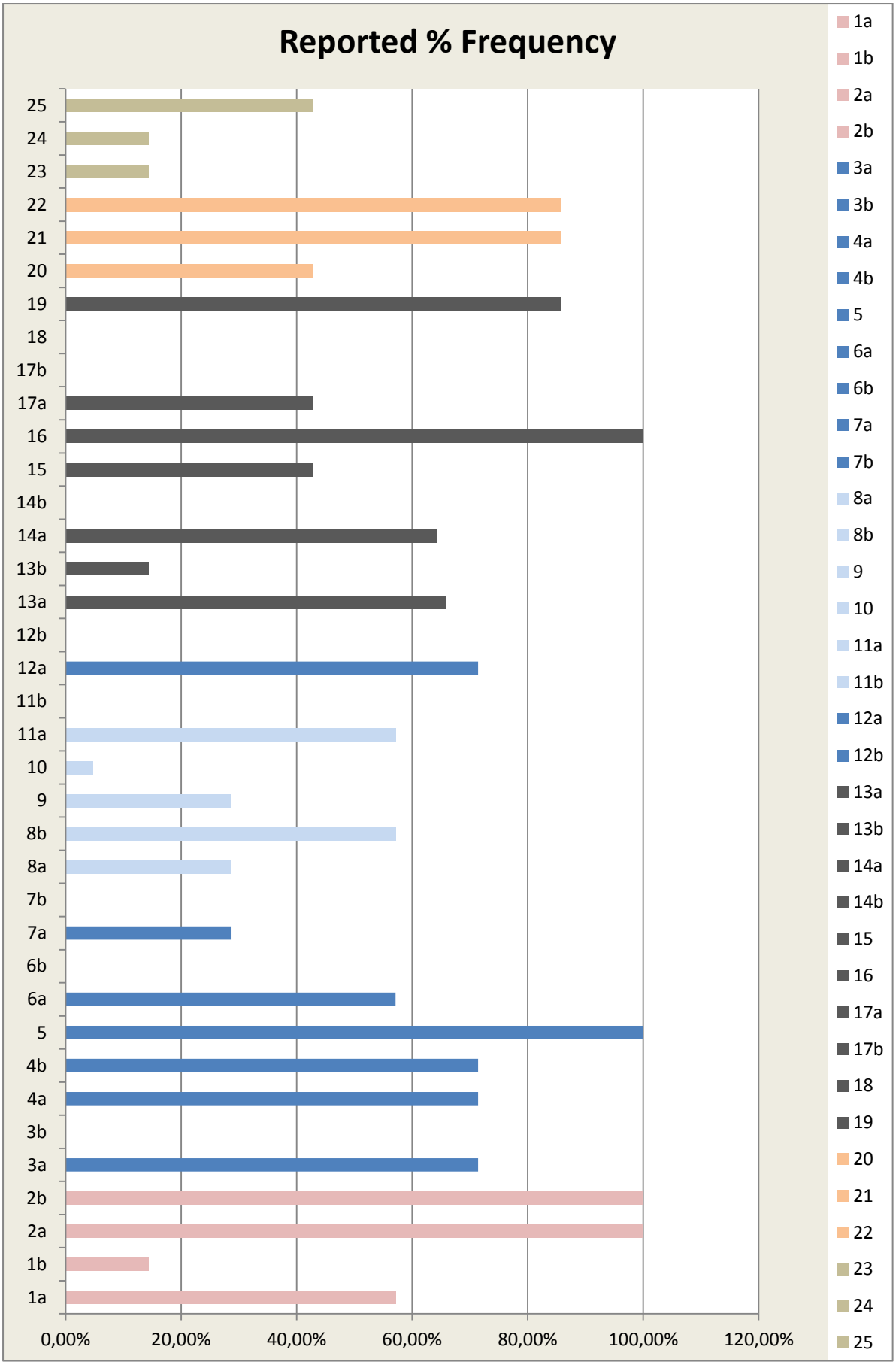


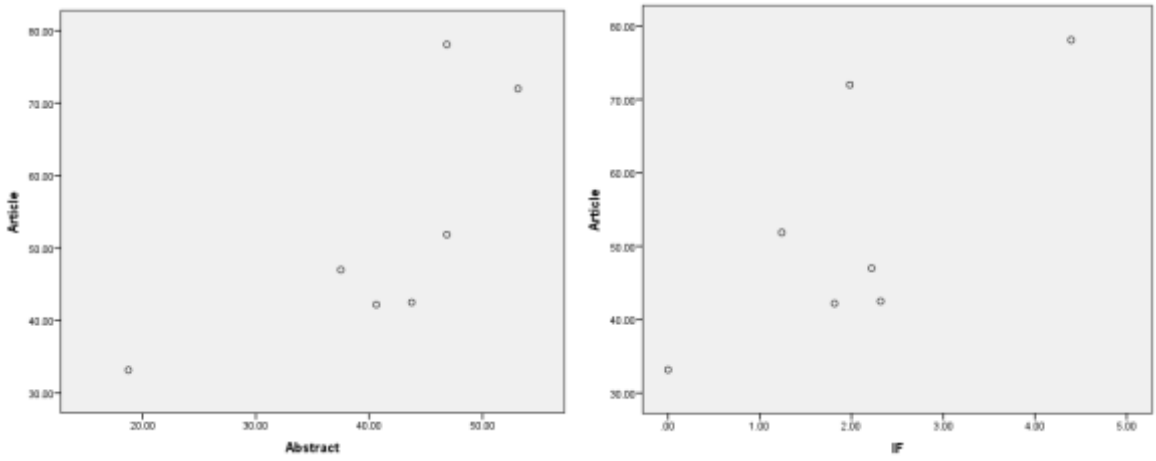
Figure 3 Compliance per CONSORT item



**Journal Ranking**

The Spearman's rho between CONSORT and journals' IF was (0.571, p-value=0.180>0.05), which is suggestive of a moderate positive correlation, but is not statistically significant. We determined the Pearson's r (IF were normally distributed) without taking the study of Chitsaz et al into consideration (ESCI). The result was not statistically significant (0.627, p-value=0.183).

Figure 4 I Trends between Article and Abstract reporting quality / reporting quality and journal ranking




In the second chart the study of Chitsaz at al is featured. Since it was published in a journal indexed in the ESCI it was conventionally attributed an impact factor of 0.

**Reporting Quality of Abstracts**

We evaluated the reporting quality of each abstract based on the CONSORT for Abstracts extension. The following results were obtained: mean=41.07, sd=11.04, median=43.75 min&max=18.75&53.13

Amiri at al: (6/16, 37.5%), Su et al (7.5/16, 46.86%), Chitsaz et al (3/16, 18.75%), Malamiri et al (8.5/16, 53.13%), Gilad et al (7/16, 43.75%), Mehta et al: (7.5/16, 46.86%), Agarwal et al: (6.5/16, 40.63%)

The Spearman's rho between CONSORT adherence and adherence to the CONSORT extension for abstracts was calculated (0.829, p-value=0.021<0.05). The result was indicative of a strong positive correlation between abstract and article reporting quality and was statistically significant. Pearson's r (Shapiro-Wilk test compatible with normal distribution for both variables) was also determined (0.737, p-value=0.059>0.05), but the result was not statistically significant.

**Reporting Quality of Pilot Trials**

The literature search we performed provided four Pilot trials [35-38]. CONSORT compliance was assessed:

Misra et al 2006: (10.83/33, 32.82%), Chen et al: (20.5/33, 62.12%), Mundlamuri et al (19.83/33, 60.1%), Misra et al 2017 (21.5/33, 65.15%)

The mean CONSORT adherence was calculated at 55.05% with sd=7.48. The median was 61.11% and the minimum and maximum adherence 32.82% and 65.15% respectively. Item 1b was appraised as reported in only one trial (with a score of 7.5/15).

Mann-Whitney U test determined than CONSORT adherence was similar between RCTs and Pilot trials, p-value=0.85 (according to Shapiro-Wilk test figures from Pilot trial assessment were not normally distributed, p-value=0.45).

# Conclusions

We evaluated the reporting quality of RCTs for sodium valproate in status epilepticus according to the 2010 CONSORT statement. Our review included all RCTs published between 2007 and 2018. 7 eligible studies were assessed for adherence to the CONSORT statement. The overall reporting quality was rather poor (52.40%) with solely 2 studies reporting above 70% of the CONSORT items. Reporting essential CONSORT items, relating to methodological features and results, was notably insufficient, complicating the interpretation of the studies. In contrast, elaboration of the study background and discussion of the study results were sufficiently reported.

Our study attempted to investigate correlations between adherence to the CONSORT statement and adherence to the CONSORT extension for abstracts as well as journal ranking. It is crucial that abstracts of RCTs constitute well structured and accurate summaries of the study. Readers commonly decide to acquire or not articles based on the quality of abstracts, owing to the overabundance of publications in most fields [(39)]. It is not our purpose to determine if there is a need for optimisation in the CONSORT compliance of abstracts, but rather to establish if the reporting quality of abstracts is indicative of the reporting quality of RCTs. Our analysis included both parametric and non-parametric methods. Despite the fact that data followed normal distribution according to the Shapiro-Wilk test, it would not be prudent to ignore the small sample size. Results from both analyses were suggestive of strong positive correlation, with Spearman's rho reaching statistical significance and Pearson's r falling short of significance. The study of Jeroen P. M. Peters et al [(40)] determined CONSORT compliance of both full-texts and abstracts in otorhinolaryngologic literature, but did not investigate for correlations between them.

IF is considered by many as a marker of journal quality and consequently, article quality [(41)]. Correlation between adherence to the CONSORT statement and journals ranking was also determined by both parametric and non-parametric methods, both of which were indicative of moderate correlation, but without achieving statistical significance. This correlation has been studied by multiple reviews [(42-46)], some of which were able to identify significant correlation [(44-46)].

Pilot trials are considered preliminary studies [(47)]. They are conducted on a smaller scale than the main study in order to assess the feasibility (design, recruitment, randomization, blinding) of a larger full-scale study. At the same time, researchers gather evidence regarding the efficacy and adverse effects of an intervention [(48)]. Therefore it is comprehensible that transparent reporting of Pilot RCTs is of crucial importance for researchers to recreate a concluding study or to assemble evidence as part of a meta-analysis. The literature search we performed identified four Pilot studies, a number of studies comparable to the number of RCTs. Therefore, we decided to appraise the reporting quality of the Pilot trials retrieved. A slightly greater, but insignificant, CONSORT compliance was observed.

Many other parameters have been proposed as possible determinants of the reporting quality of RCTs. Liu et al [(42)], as well as Plint et al [(49)] analysed the role of CONSORT endorsement and concluded that reporting quality is superior in journals that endorse the CONSORT statement . On the grounds

that scientific collaboration is sometimes accountable for higher quality studies[50] the number of authors has been proposed as a possible determinant of reporting quality[43, 46], without significant results supporting this claim. Stevanovic et al [44] obtained significant results from the correlation of CONSORT adherence and citation count per article. Single or multi-centre design [50] is not considered an important factor. Sample size[42,50], publication date[43, 51] and funding of a study[42, 50, 51] have also been analysed, with outcomes being contradictory.

Reporting of the methodological items is probably the most crucial segment of the CONSORT statement. There is a number of studies that focuses primarily on methodological features since their optimization is considered most important[52-54]. We obtained disappointing results regarding reporting quality of methodological features, which appears to be a scourge on reporting quality of RCTs in general.

Wu et al[23] and McMullan et al[24] made an effort to review the reporting quality of RCTs for benzodiazepines (first line AEDs) in SE as part of meta-analyses. Wu et al reviewed studies between lorazepam or diazepam from 1966 to February 2014. 6 eligible studies were assessed based on a 22 item list and the proportion of reported items (10, 11, 13, 13, 15, 18) was assessed as satisfactory. McMullan et al reviewed RCTs between midazolam and diazepam. The CONSORT reporting tool was deployed in a form of a 30-item list and a threshold score of at least 20 was established for inclusion. Among the 14 eligible studies 8 were attributed a CONSORT score of 15-19, whereas 6 were attributed a CONSORT score above 20 (22, 23, 24, 26, 27, 28). Both studies recorded superior reporting qualities in comparison with our findings.

To our knowledge, our study is the first to assess the reporting quality of studies in the field of second line AEDs in the treatment of SE. We divided each CONSORT item into sections in order to establish a more accurate reporting tool. It is appropriate to point out that our study has certain limitations. First of all, our research provided a small number of RCTs. Secondly, each RCT was assessed by a single researcher. In addition to that, the researcher was not blinded to information in regards to authorship, country of origin and journal in which the article was published. Furthermore, we reviewed exclusively studies published in English. Having said all these, we would like to highlight the importance of carrying out a study for evaluation of the reporting quality of RCTs in their initial form of submission in comparison with the published form, so as to investigate the improvement of reporting thanks to the revisions prior to publication.

It is of critical importance to keep in mind that reporting quality is not identical to procedural quality. The capitalization of accurate reporting lies in the reader's aptitude for interpretation.

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